Gene transfer into the lung by nanoparticle dextran-spermine/plasmid DNA complexes.

ABSTRACT

A novel cationic polymer, dextran-spermine (D-SPM), has been found to mediate gene expression in a wide variety of cell lines and in vivo through systemic delivery. Here, we extended the observations by determining the optimal conditions for gene expression of D-SPM/plasmid DNA (D-SPM/pDNA) in cell lines and in the lungs of BALB/c mice via instillation delivery. In vitro studies showed that D-SPM could partially protect pDNA from degradation by nuclease and exhibited optimal gene transfer efficiency at D-SPM to pDNA weight-mixing ratio of 12. In the lungs of mice, the levels of gene expression generated by D-SPM/pDNA are highly dependent on the weight-mixing ratio of D-SPM to pDNA, amount of pDNA in the complex, and the assay time postdelivery. Readministration of the complex at day 1 following the first dosing showed no significant effect on the retention and duration of gene expression. The study also showed that there was a clear trend of increasing size of the complexes as the amount of pDNA was increased, where the sizes of the D-SPM/pDNA complexes were within the nanometer range.

Keyword: Gene expression; Dextran-spermine (D-SPM); Nanoparticle; Spermine; Plasmid DNA; Lung.